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(56) Documents cited
Chem. Abstr., Vol. 103, No 22585s
Chem. Abstr., Vol 98, No 126074u
J. Med. Chem., Vol. 27, No 11, 1984, pages 1396 to 1400

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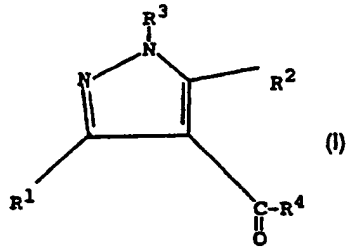
(54) Fungicidal pyrazolyl aryl ketones

(57) A *method of combating fungus* at a locus, characterised by treating the locus with a fungicidally effective amount of a compound of general formula



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[in which R^1 represents an alkyl group;
R^2 represents a halogen atom, or an optionally substituted amino group (including alkylamino, alylamino and acylamino)
R^3 represents an alkyl group; and
R^4 represents an optionally substituted aryl group;
including any such compounds in the form of N-oxides and acid addition salts] and compositions containing such compounds in combination with a surface-active agent are disclosed.

Compounds of formula I wherein R^1 and R^3 are both methyl, R^2 is NH_2 and R^4 is either 2, 4-dichlorophenyl or 2,6-dichlorophenyl (and acid addition salts thereof) and processes for their preparation are novel.

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FUNGICIDAL COMPOUNDS

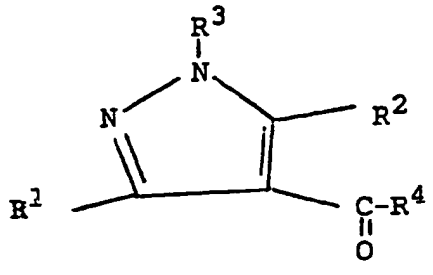
This invention relates to the use of certain pyrazolyl aryl ketones as fungicides, to fungicidal compositions containing such compounds, and to certain novel compounds and their preparation.

In J. Org. Chem., vol. 36, No.17, 1971, p.2542 et seq, there is described a number of 1,3-dialkyl-5-chloropyrazol-4-yl aryl ketones. However, no use is proposed for the compounds.

In J. Med. Chem. 1984, 27, p.1396-1400 et seq, there is described a number of (1,3-dialkyl-5-amino-1H-pyrazol-4-yl) aryl methanones. Pharmacological evaluation is said to demonstrate central nervous system depressant activity, and potential anti-convulsant properties. However, no fungicidal activity is suggested.

The present invention is based upon the unexpected discovery of fungicidal activity of (1,3-dialkyl-1H-pyrazol-4-yl) phenyl methanones.

According to the present invention there is provided a method of combating fungus at a locus, characterised by treating the locus with a fungicidally effective amount of a compound of general formula



(I)

in which R^1 represents an alkyl group;
R^2 represents a halogen atom, or an optionally substituted amino group;
R^3 represents an alkyl group; and
R^4 represents an optionally substituted aryl group.

Included within the scope of the invention are such compounds in the form of their N-oxides and acid addition salts, where possible.

Unless otherwise specified in this specification, an alkyl group may be linear or branched and may and may contain up to 10, preferably up to 6, and most preferably up to 4, carbon atoms, suitable examples being methyl, ethyl and propyl.

When any groups are designated as being optionally substituted, the substituent groups which are optionally present may be any of those customarily employed in the development of pesticidal compounds, and/or the modification of such compounds to influence their structure/activity, persistence, penetration or other property. In relation to an aryl moiety, optional substituents include halogen, especially fluorine, chlorine and bromine atoms, and nitro, cyano, amino, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl (especially CF_3), C_{1-4} alkoxy and phenoxy groups. 1 to 3 substituents may be suitably employed. In the case of an optionally substituted amino group R^2, substituents are preferably selected from alkyl, acyl, aryl and amino groups.

The term "acyl" is used to denot a radical d rived from an organic acid by the removal of a hydroxyl group; the organic acid may be a carboxylic acid

(including carbamic acid derivatives) or a sulphonic acid, examples of suitable acyl groups being groups of the formula $-COR_5$ or $-SO_2R_5$ wherein R_5 represents a hydrogen atom or an alkyl group. A preferred acyl group is $-COR_5$, especially formyl.

Preferably, R^1 and R^3 both represent methyl groups.

Preferably, R^2 represents a chloro atom, an amino group or an amino group substituted by one group selected from alkyl, preferably methyl, and acyl, preferably formyl. Most preferably, R^2 represents an amino group (NH_2).

R^4 preferably represents a phenyl group having one or two substituents selected from halogen atoms (preferably fluorine or, especially, chlorine), C_{1-4} haloalkyl groups (preferably trifluoromethyl), C_{1-4} alkyl groups (preferably methyl), C_{1-4} alkoxy groups (preferably methoxy), and phenoxy groups. Of these, most preferred are chlorine atoms and alkoxy groups.

When R^4 is substituted it preferably has a substituent in the 2- position (and is optionally substituted elsewhere).

An acid addition of a compound of formula I is preferably a hydrohalide salt, preferably hydrochloride. Pr ferably, however, th compound of formula I used in the method of the invention is neither in the form of an N-oxide nor an acid addition salt.

In the method according to the invention the locus preferably comprises plants subject to or subjected

to fungal attack, seeds of such plants, or the medium in which the plants are growing or are to be grown. The plants are preferably cereal plants, especially barley. The method of the invention is particularly effective in combating powdery mildews of cereal plants, for example barley powdery mildew.

The locus may conveniently be treated with the compound I at an application rate in the range 0.05-4 kg/ha, preferably 0.1-1kg/ha.

The invention also provides the use of a compound of formula I as defined as a fungicide.

Further with accordance with the invention there is provided a fungicidal composition comprising an active ingredient of general formula I, as defined above, in association with at least two carriers, at least one of which is a surface-active agent.

A composition according to the invention preferably contains from 0.5 to 95% by weight of active ingredient.

A carrier in a composition according to the invention is any material with which the active ingredient is formulated to facilitate application to the locus to be treated, which may for example be a plant, seed or soil, or to facilitate storage, transport or handling. A carrier may be a solid or a liquid, including a material which is normally gas ous but which has b en compress d to form a liquid, and any of th carriers normally used in formulating pesticidal compositions may be used. Preferably compositions according to the invention contain 0.5 to 95% by weight of active ingr dient.

Suitable solid carriers include natural and synthetic clays and silicates, for example natural silicas such as diatomaceous earths; magnesium silicates, for example talcs; magnesium aluminium silicates, for example attapulgites and vermiculites; aluminium silicates, for example kaolinites, montmorillonites and micas; calcium carbonate; calcium sulphate; ammonium sulphate; synthetic hydrated silicon oxides and synthetic calcium or aluminium silicates; elements, for example carbon and sulphur; natural and synthetic resins, for example coumarone resins, polyvinyl chloride, and styrene polymers and copolymers; solid polychlorophenols; bitumen; waxes; and solid fertilizers, for example superphosphates.

Suitable liquid carriers include water; alcohols, for example isopropanol and glycols; ketones, for example acetone, methyl ethyl ketone, methyl isobutyl ketone and cyclohexanone; ethers; aromatic or araliphatic hydrocarbons, for example benzene, toluene and xylene; petroleum fractions, for example kerosene and light mineral oils; chlorinated hydrocarbons, for example carbon tetrachloride, perchloroethylene and trichloroethane. Mixtures of different liquids are often suitable.

Agricultural compositions are often formulated and transported in a concentrated form which is subsequently diluted by the user before application. The presence of small amounts of a carri r which is a surface-active ag nt facilitates this proc ss of dilution. Thus pr ferably at l ast on carri r in a composition according to the inv ntion is a surface-active agent. For example the composition may contain at least two carri rs, at least one of which is a surface-

active agent.

A surface-active agent may be an emulsifying agent, a dispersing agent or a wetting agent; it may be nonionic or ionic. Examples of suitable surface-active agents include the sodium or calcium salts of polyacrylic acids and lignin sulphonic acids; the condensation of fatty acids or aliphatic amines or amides containing at least 12 carbon atoms in the molecule with ethylene oxide and/or propylene oxide; fatty acid esters of glycerol, sorbitol, sucrose or pentaerythritol; condensates of these with ethylene oxide and/or propylene oxide; condensation products of fatty alcohol or alkyl phenols, for example p-octylphenol or p-octylcresol, with ethylene oxide and/or propylene oxide; sulphates or sulphonates of these condensation products; alkali or alkaline earth metal salts, preferably sodium salts, of sulphuric or sulphonic acid esters containing at least 10 carbon atoms in the molecule, for example sodium lauryl sulphate, sodium secondary alkyl sulphates, sodium salts of sulphonated castor oil, and sodium alkylaryl sulphonates such as dodecylbenzene sulphonate; and polymers of ethylene oxide and copolymers of ethylene oxide and propylene oxide.

The compositions of the invention may for example be formulated as wettable powders, dusts, granules, solutions, emusifiable concentrates, emulsions, suspension concentrates and aerosols. Wettable powders usually contain 25, 50 or 75% w of active ingredient and usually contain in addition to solid inert carrier, 3-10% w of a dispersing agent and, wher necessary, 0-10% w of stabiliser(s) and/or oth r additiv s such as penetrants or stickers. Dusts ar usually formulated as a dust concentrat having a similar composition to that of a

wettable powder but without a dispersant, and are diluted in the field with further solid carrier to give a composition usually containing 0.5-10% w of active ingredient. Granules are usually prepared to have a size between 10 and 100 BS mesh (1.676 - 0.152 mm), and may be manufactured by agglomeration or impregnation techniques. Generally, granules will contain 0.5-75% w active ingredient and 0-10% w of additives such as stabilisers, surfactants, slow release modifiers and binding agents. The so-called "dry flowable powders" consist of relatively small granules having a relatively high concentration of active ingredient. Emulsifiable concentrates usually contain, in addition to a solvent and, when necessary, co-solvent, 10-50% w/v active ingredient, 2-20% w/v emulsifiers and 0-20% w/v of other additives such as stabilisers, penetrants and corrosion inhibitors. Suspension concentrates are usually compounded so as to obtain a stable, non-sedimenting flowable product and usually contain 10-75% w active ingredient, 0.5-15% w of dispersing agents, 0.1-10% w of suspending agents such as protective colloids and thixotropic agents, 0-10% w of other additives such as defoamers, corrosion inhibitors, stabilisers, penetrants and stickers, and water or an organic liquid in which the active ingredient is substantially insoluble; certain organic solids or inorganic salts may be present dissolved in the formulation to assist in preventing sedimentation or as anti-freeze agents for water.

Aqu ous dispersions and emulsions, for example compositions obtain d by diluting a wettable powder or a concentrate according to the invention with wat r, also lie within the scope of the invention. The said mulsions may be of the water-in-oil or of the oil-in-water type, and may have a thick "mayonnaise" - like

consistency.

The composition of the invention may also contain other ingredients, for example other compounds possessing herbicidal, insecticidal or fungicidal properties.

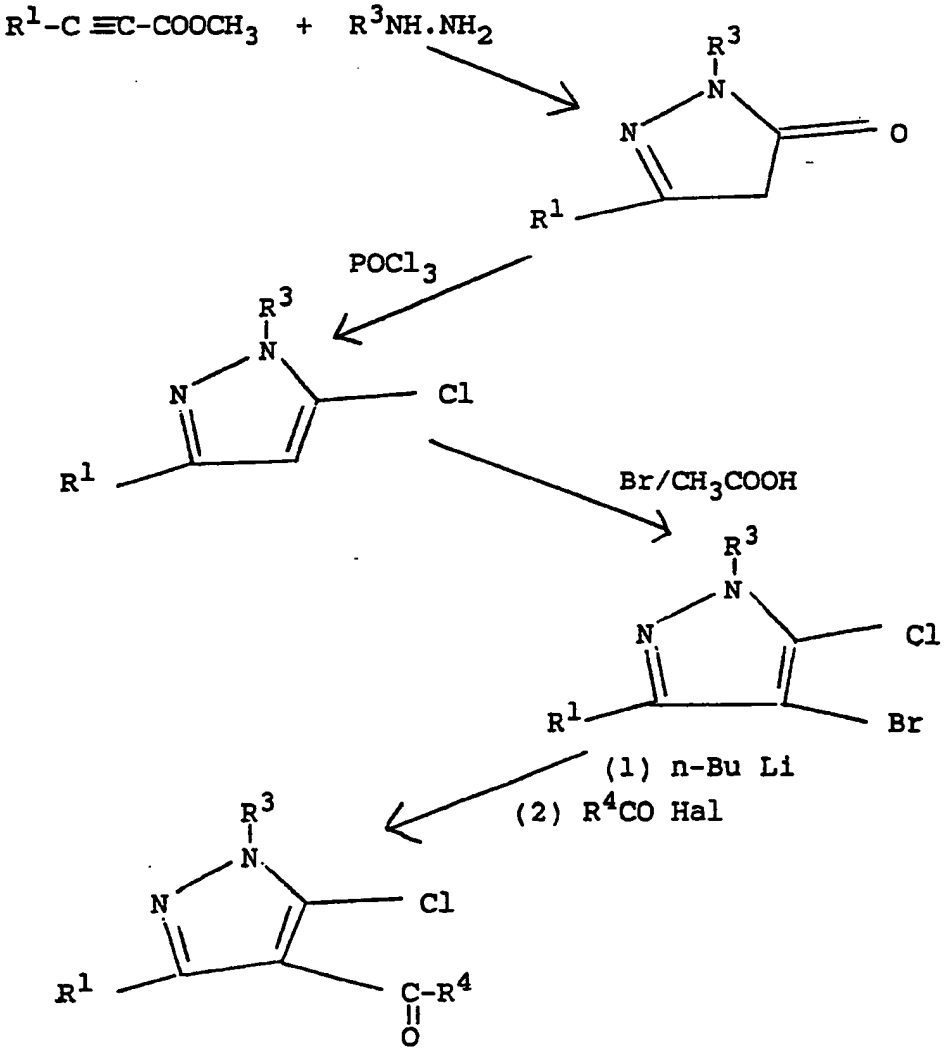
The most active compounds of the present invention are believed to be compounds of formula I wherein R^1 and R^3 are both methyl, R^2 is amino, and R^4 is 2,4- or 2,6-dichlorophenyl; together with acid addition salts thereof. Such compounds are novel and constitute a further aspect of the invention.

Compounds of formula I may be prepared by various methods, as described in the two prior art references mentioned above, and in J. Am. Chem. Soc., 81, p.2465 et seq, (1959), and in the documents referenced in these documents.

In one preferred method, the appropriate 1,3-dialkyl-5-aminopyrazole (for example, prepared in accordance with the method described in J.Am. Chem. Soc., 81, p.2456 et seq., (1959), or its acid addition salt, is aroylated by a compound R^4CO-Hal, where Hal represents a halogen, preferably chlorine atom, under Friedel-Crafts conditions, and the aroylamino product is treated under acid hydrolysis conditions, in accordance with the method described in J.Med. Chem., 27., p.1396 et seq., (1984). The first step preferably takes place using $AlCl_3$ as catalyst, a halogenated hydrocarbon, suitably 1,1,2,2-tetrachloro thane, as solvent, at an el vated temperature, pr ferably und r r flux. The s cond st p pr ferably at elevated temperatur , suitably following additions of a hydrohalic acid (for exampl , hydrobromic acid) and glacial acetic acid.

The product is the hydrohalide salt of the 1,3-dialkyl-5-aminopyrazol-4-yl-arylmethanone. This may be converted into further compounds of formula I, for example by treatment with a base to remove HBr, and by reaction with an acylating agent to yield an N-acyl derivative (for example, with formic acetic anhydride, to yield the N-formyl derivative).

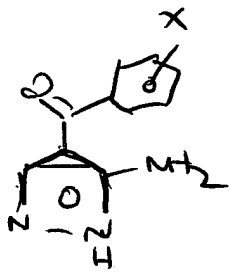
In a further preferred method a compound of formula I in which R^2 represents a halogen, preferably chlorine, atom is prepared by the following route:



The 4-bromo-5-chloro-1,3-dialkylpyrazole compound shown above is treated with n-butyl lithium and the resultant 4-lithiopyrazole is mixed with an anhydrous ethereal solution of an appropriate aroyl halide, preferably chloride.

The product may be converted into further compounds of formula I, for example by treatment with ammonium hydroxide at elevated temperature and pressure (for example, 100-200°C in an autoclave), or with an alkylamine in a polar organic solvent, at a temperature in the range 10-50°C, to produce the (alkyl)amino analogue, or with a mineral acid to yield the acid addition salt.

Such preferred methods, as applied to the preparation of novel compounds of formula I, constitute a further aspect of the present invention.



The invention is further illustrated by the following Examples.

Example 1

Preparation of (1,3-dimethyl-5-amino-1H-pyrazol-4-yl) -2,4-dichlorophenyl methanone

A suspension of aluminium chloride (0.25M, 33.5g) in 1,1,2,2-tetrachloroethane (200ml) was cooled to 0-5°C and 2,4-dichlorobenzoyl chloride (0.35M, 73.3g) followed by 1,3-dimethylpyrazol-5-amine hydrochloride (0.1M, 14.8g) was added. Th mixture was stirr d under reflux for 18 hours, cooled and added to 1.17M hydrochloric acid (500ml). After stirring for one hour the organic layer was s parated and washed with dilut ammonium hydroxide follow d by water. Solvent was removed and th residue dissolved in a mixture of 48%

hydrobromic acid (225ml) and glacial acetic acid (75ml). The mixture was refluxed for 18 hours, cooled and about half of the solvent removed in vacuo. The insoluble white precipitate of the hydrobromide salt was recovered by filtration and washed with dichloromethane (Yield 10.1g, 28%). Treatment of the hydrobromide salt (2.0g, 5.5mM) with excess 2M sodium hydroxide followed by ether extraction yielded the title compound as a yellowish solid, m.p. 62-65°C.

Analysis

Calculated	:	50.7	3.9	14.8	% CHN
Found	:	50.5	4.1	14.4	

Example 2

Preparation of (1,3-dimethyl-5-amino-1H-pyrazol-4-yl) 2,6-dichlorophenyl methanone

A mixture of (5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)-2,6-dichlorophenyl-methanone (0.01M, 3.0g), (prepared in accordance with the methods described in J.Med. Chem., (1984) 27, p.1396 et seq., and J.Am. Chem. Soc., (1959) 81, p.2456 et seq,) and 30% ammonium hydroxide (50ml) was heated to 155-160°C in a glass lined stainless steel autoclave for 18 hours. The cooled mixture was extracted with ether (2 x 50ml) and the combined extracts washed with dilute aqueous sodium hydroxide, then water. After drying over $MgSO_4$ the solvent was evaporated to leave a yellowish residue which was purified by recrystallisation from benzene/60/80 petrol mixture to afford the title compound (1.6g, 56%) as an off-whit solid, m.p.177-179°C.

Analysis

Calculat d	:	50.7	3.9	14.8	% CHN
Found	:	50.9	4.0	14.8	

Further compounds were prepared according to procedures similar to those described above. Data on these compounds are set out in Table 1 below, in which the compounds described are in accordance with the general formula

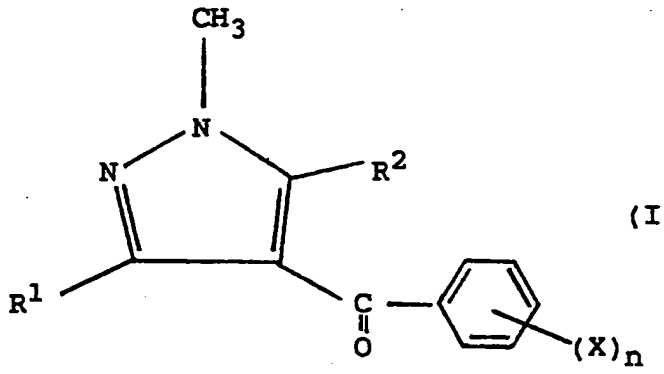


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TABLE 1

Ex.	R^1	R^2	$(X)_n$	mp(°C)	Analysis % C H N	Calc. Found
3	CH_3	$NH_2.HCl$	2-Cl	N.A.	50.3, 4.5, 14.7 49.5, 4.3, 13.9	
4	CH_3	NH_2	2,6-F_2	145	57.4, 4.4, 16.7 57.5, 4.3, 17.6	
5	CH_3	$NH_2.HCl$	2,6-F_2	196	N.A.	
6	CH_3	NH_2	4-Cl	158	57.7, 4.8, 16.8 57.7, 4.9, 16.8	
7	CH_3	$NH_2.HCl$	3-OPh	92	62.9, 5.2, 12.2 63.6, 5.9, 11.0	
8	CH_3	$NH_2.HBr$	2,4-Cl_2	222	39.5, 3.3, 11.5 37.7, 3.7, 11.2	
9	CH_3	$NH_2.HCl$	2-CH_3	216	58.8, 6.0, 15.8 59.0, 6.1, 15.8	
10	CH_3	NH_2	4-CH_3	131	68.1, 6.6, 18.3 68.2, 6.5, 17.4	
11	CH_3	NH_2	3-CF_3	oil	55.1, 4.2, 14.8 55.2, 4.8, 13.6	
12	CH_3	$NH_2.HCl$	4-OCH_3	95	55.4, 5.7, 14.9 55.8, 5.9, 15.0	

N.A. = NOT AVAILABLE

TABLE 1 Continued)

Ex.	R^1	R^2	$(X)_n$	mp(°C)	Analysis % C H N	Calc. Found
13	CH_3	$NH_2.HCl$	2-OCH_3	164	55.4, 5.7, 14.9 55.3, 5.8, 15.3	
14	$CH_3CH_2CH_2$	$NH_2.HCl$	2,6-Cl_2	205	48.2, 4.6, 12.1 49.5, 4.7, 12.4	
15	CH_3	NHCHO	2,4-Cl_2	N.A.	50.0, 3.6, 13.5 48.7, 3.7, 12.7	
16.	CH_3	$NHCH_3$	2,4-Cl_2	130	52.5, 4.0, 14.1 53.3, 4.7, 14.0	
17	CH_3	Cl	2,6-Cl_2	78	47.5, 3.0, 9.2 44.1, 3.0, 9.8	
18	CH_3	Cl	4-OCH_3	129	59.0, 4.9, 10.6 59.0, 5.2, 11.0	
19	CH_3	Cl	2-OCH_3	89	59.0, 4.9, 10.6 59.6, 4.9, 10.5	
20	$CH_3CH_2CH_2$	Cl	2,6-Cl_2	N.A.	N.A.	
21	CH_3	Cl	2,4-Cl_2	94	47.5, 3.0, 9.2 47.2, 3.1, 8.3	

N.A. = NOT AVAILABLE

Fungicidal Activity

The fungicidal activity of compounds of the invention was investigated by means of the following tests.

(a) Direct protectant activity against vine downy mildew (Plasmopara viticola; Pvp)

The test is a direct protectant one, using a foliar spray. The lower surfaces of leaves of whole vine plants (cv Cabernet Sauvignon) are sprayed with a solution of active material in 1:1v/v water/acetone containing 0.04%w "Triton X-155" (registered trade mark) (octylphenol polyoxyethylene surfactant), at a dosage of 1 kilogram of active material per hectare using a track sprayer which delivers 620 litres/ha, and after a subsequent 24 hours under normal glasshouse conditions the lower surfaces of the leaves are inoculated by spraying with an aqueous solution containing 10^4 zoosporangia/ml. The inoculated plants are kept for 24 hours in a high humidity compartment, 5 days under normal glasshouse conditions and then returned for a further 24 hours to high humidity. Assessment is based on the percentage of leaf area covered by sporulation compared with that on control leaves.

(b) Antisporulant activity against vine downy mildew (Plasmopara viticola; Pva)

Th test is a direct antisporulant on using a foliar spray. The lower surfaces of leaves of whole vin plants (cv Cabernet Sauvignon) are inoculated by spraying with an aqueous suspension containing 10^4 zoosporangia/ml

2 days prior to treatment with the test compound. The inoculated plants are kept for 24 hours in a high humidity compartment, and then 24 hours at glasshouse ambient temperature and humidity. When the plants are dry, infected leaves are sprayed on their lower surfaces with a solution of active material in 1:1 water/acetone containing 0.04% w/w "Triton X-155" (trade mark) (an octylphenol polyethoxylate surfactant). The spraying is carried out with a moving track sprayer with delivers 620 litre/ha, and the concentration of active material is calculated to give an application rate of 1kg/ha. After spraying, the plants are returned to normal glasshouse conditions for 96 hours and are then transferred to the high humidity compartment for 24 hours to induce sporulation, prior to assessment. Assessment is visual and is based on the percentage of the leaf area covered by sporulation compared with that on control leaves.

(c) Activity against wheat leafspot (Leptosphaeria nodorum; Ln)

The test is a direct antisporulant one, using a foliar spray. Leaves of wheat plants (cv Mardler), at the single leaf stage, are inoculated by spraying with an aqueous suspension containing 8×10^5 spores/ml. The inoculated plants are kept for 24 hours in a high humidity compartment prior to treatment. The plants are sprayed at a dosage of 1 kg. of active material per hectare using a track sprayer as described under (a). After drying, the plants are kept for 5 days under normal glasshouse conditions, followed by assessment. Assessment is based on the percentage of leaf area covered by sporulation compared with that on leaves of control plants.

(d) Activity against barley powdery mildew (Erysiphe graminis f.sp. hordei; Eg)

The test is a direct antisporulant one, using a foliar spray. Leaves of barley seedlings, cultivar Golden Promise, are inoculated by dusting with mildew conidia one day prior to treatment with the test compound. The inoculated plants are kept overnight at glasshouse ambient temperature and humidity prior to treatment. The plants are sprayed at a dosage of 1kg. of active material per hectare using a track sprayer as described under (a). After drying, plants are returned to a compartment at ambient temperature and humidity for up to 7 days, followed by assessment. Assessment is based on the percentage of leaf area covered by sporulation compared with that on leaves of control plants.

(e) Activity against apple powdery mildew (Podosphaera leucotricha; Pl)

The test is a direct anti-sporulant one using a foliar spray. The upper surfaces of leaves of whole seedlings are inoculated by spraying with an aqueous suspension containing 10^5 conidia/ml 2 days prior to treatment with the test compound. The inoculated plants are immediately dried and kept at glasshouse ambient temperatures and humidity prior to treatment. The plants are sprayed at a dosage of 1 kilogram of active material per hectare using a track sprayer as described under (a). After drying the plants are returned to a compartment at ambient temperature and humidity for up to 9 days, follow d by ass ssment. Ass ssment is based on the p rcentage of the l af area cov red by sporulation compared with that on l aves of control plants.

(f) Activity against wheat eyespot (Pseudocereosporella herpotrichoides;Ph).

The test is an in vitro one. Samples are prepared wherein 0.7 mls solution containing 2 mg active material dissolved in acetone is evenly dispersed in 20ml molten half-strength potato dextrose agar (formed by dissolving 2g potato extract, 10g dextrose and 7.5g agar in 1 litre of water and sterilising for 15 minutes at 121°C) and the resulting 20ml portions are allowed to set in 9cm petri dishes. The concentration of active material in the resulting samples is 100ppm. Upon setting, two plugs of 5mm diameter taken from the advancing edge of a stock plate of a 3 to 4 week old culture of P.herpotrichoides on full strength potato dextrose agar, incubated at 20-22°C in darkness, are placed, equally spaced on the surface of each sample, mycelial side uppermost. The samples are incubated for 11 days at 20-22°C in darkness before assessment. Diametric growth is measured with the width of the plug subtracted and results compared with growth on a sample wherein 0.7ml acetone containing no active material is dispersed in 20ml half-strength potato agar.

(g) Activity against seedling wheat blight (Fusarium culmorium; Fc)

The test is an anti-sporulant one using a soil drench. Surface sterilised wheat seeds (var Waggoner) are inoculated by soaking in an aqu ous suspension containing 7 x 10^5 spor s/ml (60mg s ed per 80ml suspension) at 22°C for 6 hours. The se ds ar then sown in pots (5 per pot) in sand at a d pth of 1cm. 1 day after inoculation and planting the active mat rial is appli d at a rate of 10kg/ha by pouring on a soil dr nch

(concentration 0.36g/l active material in 12%v/v acetone/water) evenly over the sand. The pots are then transferred to glasshouse, kept at 25°C and watered sparingly. 21 days after inoculation the resulting seedlings are removed from the pots and their roots are gently washed. Visual assessment is made based on lesion development on stem base and upper roots in comparison with control seedlings.

(h) Activity against broad bean rust (Uromyces fabae Uf)

The test is a translaminar antisporulant one using foliar spray. Pots containing 1 plant per pot were inoculated by spraying an aqueous suspension, containing 5×10^4 spores/ml plus a little "Triton X-155" (trade mark), onto the undersurface of each leaf 20-24 hours before treatment with test compound. The inoculated plants were kept overnight in a high humidity compartment, dried at glasshouse ambient temperature and then sprayed, on the leaf upper surface, at a dosage of 1kg/ha of active material using a track sprayer as described under (a). After treatment the plants were kept at glasshouse temperature and assessment made 11-14 days after treatment. Symptoms are assessed on the relative density of sporulating pustules per plant compared with that on control plants.

(i) Activity against wheat brown rust Puccinia Recondita; Pr)

Th t st is a dir ct protectant one using a foliar spray. Wheat seedlings (cv Brigand) are grown to the 1-1.5 l af stage. Th plants ar th n spray d with the test compound at a dosage of 1 kg/ha using a track

sprayer as described under (a). Test compounds are applied as solutions or suspensions in a mixture of acetone and water (50:50 $^{v}/_{v}$) containing 0.04% surfactant ("TWEEN 20" - Registered Trade Mark).

18-24 hours after treatment, the seedlings are inoculated by spraying the plants from all sides with an aqueous spore suspension containing about 10^5 spores/ml. For 18 hours after inoculation, the plants are kept in high humidity conditions at a temperature of 20-22°C. Thereafter, the plants are kept in ambient glasshouse conditions, that is, in moderate relative humidity and at a temperature of 20°C.

The disease is assessed 10 days after inoculation on the basis of the percentage of the plant covered by sporulating pustules compared with that on the control plants.

(j) Activity against Wheat root rot (Fusarium species Fs)

This test measures the in vitro activity of compounds against a species of Fusarium that causes stem and root rots.

Compound is dissolved or suspended in acetone and added to molten half strength Potato Dextrose Agar to give a final concentration of 100ppm compound and 3.5% acetone. After the agar has set, plates are inoculated with 6mm diameter plugs of agar and mycelium taken from a 7 day old culture of Fusarium sp..

Plates are inoculated at 20°C for 5 days and radial growth from the plug is measured.

Assessment in the above tests is based on a comparison between the levels of disease on the treated and untreated plants. The extent of disease control in all the above tests is expressed as a rating compared with a diluent sprayed control according to the criteria:-

0 = less than 50% disease control
1 = 50-80% disease control
2 = greater than 80% disease control

The results of the above tests are given in Table 2 following.

Table 2

Ex. No.	Fungicidal Activity Rating
1	Eg-2 Uf-1
2	Eg-2 Pvp-1
3	Eg-2 Pl-1
4	Eg-2
5	Eg-2 Ln-1
6	Fc-1 Ph-1
7	Eg-1 Pvp-1
8	Pl-2 Eg-2 Pvp-1
9	Eg-2
10	Eg-2
11	Eg-2 Pl-1
12	Pvp-1
13	Pvp-1
14	Eg-2 Pvp-1
15	Eg-2
16	Eg-2 Pvp-2 Pr-1 Fs-1
17	Eg-2 Pvp-1 Ph-1
18	Not scre ned
19	Not screened
20	Not screen d
21	Eg-2 Pva-1 Ph-1 Fs-1

Further screening was carried out to assess control of barley powdery mildew, by each of the compounds scoring the rating Eg-2 in the test described above. The activity of all of the compounds against barley powdery mildew was confirmed, with the compounds of Examples 1,9 and, especially, 2 showing particularly high activity, even at an equivalent dosage rate of 0.03Kg/ha.

The reader's attention is directed to all papers and documents which are filed concurrently with this specification, and which are open to public inspection with this specification and the contents of all such papers and documents are incorporated herein by reference.

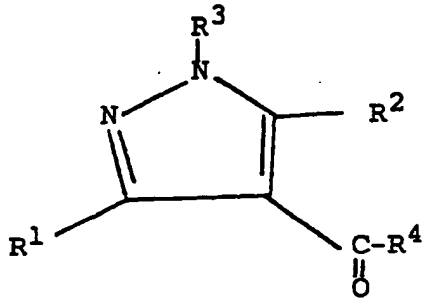
All of the features disclosed in this specification (including any accompanying claims, abstract and drawings), and/or all of the steps of any method or process so disclosed, may be combined in any combination, except combinations where at least some of such features and/or steps are mutually exclusive.

Each feature disclosed in the specification (including any accompanying claims, abstract and drawings), may be replaced by alternative features serving the same, equivalent or similar purpose, unless expressly stated otherwise. Thus, unless expressly stated otherwise, each featur disclosed is one exampl only of a generic s ries of equival nt or similar f atures.

The invention is not restricted to the details of the foregoing embodiment(s). The invention extends to any novel one, or any novel combination, of the features disclosed in this specification (including any accompanying claims, abstract and drawings), or to any novel one, or any novel combination, of the steps of any method or process so disclosed.

CLAIMS T 555 GBR

1. A method of combating fungus at a locus, characterised by treating the locus with a fungicidally effective amount of a compound of general formula



(I)

in which R^1 represents an alkyl group;
R^2 represents a halogen atom, or an optionally substituted amino group;
R^3 represents an alkyl group; and
R^4 represents an optionally substituted aryl group;
including any such compound in the form an N-oxide and acid addition salt.

2. A method as claimed in Claim 1, wherein R^1 represents a methyl group.

3. A method as claimed in Claim 1 or 2, wherein R^3 represents a methyl group.

4. A method as claimed in Claim 1, 2 or 3, wherein R^2 r pres nts a halogen at m or an amino group optionally substitut d by alkyl or acyl.

5. A method as claimed in any pr ceding claim, wh r in R^4 represents a ph nyl group having one or two substituents s lected from halogen atoms, haloalkyl,

alkyl, alkoxy and phenoxy groups.

6. A method as claimed in Claim 5, wherein R^4 represents a phenyl group having one or two substituents selected from chlorine atoms and C_{1-4} alkoxy groups.

7. A method as claimed in any preceding claim, wherein R^4 is a phenyl group having a substituent in the 2-position.

8. Use of a compound of general formula I, as defined in any of Claims 1-7, as a fungicide.

9. A fungicidal composition, comprising a compound of the general formula I, as defined in any of Claims 1-7, in association with at least two carriers, at least one of which is a surface-active agent.

10. A compound of formula I per se, as defined in any of Claims 1-7, provided that R^1 and R^3 both represent methyl groups, R^2 represents an amino group, and R^4 represents a 2,4- or 2,6-dichlorophenyl group; together with acid addition salt thereof.

11. A process for the preparation of a compound of formula I, as defined in Claim 10, wherein:

- 1,3-dimethyl-5-aminopyrazole or its acid addition salt is aroylated under Friedel-crafts conditions by a compound if formula R^4-CO-Hal, where Hal represents a halogen atom and R^4 is as defined in Claim 10; the product is subjected t acid hydrolysis conditions; and th further product is optionally treat d with a base; or

- a corresponding 1,3-dimethyl-5-halopyrazole-4-yl aryl methanon , in which R^4 is as d fin d in Claim 10,

is treated with ammonium hydroxide at elevated temperature and pressure; and the resulting 5-amino compound is optionally treated with a mineral acid to yield an acid addition salt.

12. A compound of general formula I, when produced by a process as claimed in Claim 11.

13. A method of combating a fungus at a locus and/or a fungicidal composition and/or a novel compound of formula I, and/or a process for the preparation of such a novel compound, substantially as hereinbefore described with particular reference to the Examples.